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2004-002.A101.US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Robert Alpern et al. Art Unit: 1615
Serial No.: 10/814,527
Filed: March 30, 2004
Confirmation No.: 6886
For: METHODS AND COMPOSITIONS FOR TREATMENT OF ION IMBALANCES
Examiner: Neil S. Levy

April 26, 2010

APPEAL BRIEF

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This is an appeal from the final rejection of the claims of the above-referenced application made in the Office action dated November 25, 2009. A Notice of Appeal was filed on February 25, 2010.

I. REAL PARTY IN INTEREST

The real party in interest in connection with the present appeal is Relypsa, Inc., the assignee of record.

II. RELATED APPEALS AND INTERFERENCES

Appellants are unaware of any pending appeals or interferences which may be related to, directly affect or be affected by, or have a bearing on, the Board's decision in the present appeal.

III. STATUS OF CLAIMS

Claims 1, 3, 5-11, 13-15, 36-49, 51, and 60-76 are pending. Claims 3, 5-11, 45-48, and 51 are withdrawn as they are directed to a non-elected species. Claims 2, 4, 12, 16-35, 50, and 52-59 are canceled. A copy of the pending claims appears in the Claims Appendix of this Brief.

Claims 1, 13-15, 36-44, 49, and 60-76 stand rejected under 35 U.S.C. § 112 as being nonenabled. Also, claims 1, 13-15, 36-44, 60 and 61 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Martani (EP 039453) in view of Murugesan et al (US 5,846,990) and Notenbomer (EP 0 730 494).

Applicants appeal the rejections of claims 1, 13-15, 36-44, and 60-61 under U.S.C. § 103(a) as being unpatentable.

IV. STATUS OF AMENDMENTS

No amendments were made after the final Office action. The pending claims are set out in the Claims Appendix.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The claimed subject matter is generally directed to a method of removing sodium from the gastrointestinal tract of a human patient by administering a sodium-binding polymer.

Independent claim 1 is directed to a method of removing sodium from a human subject comprising administering to a human subject in need thereof an effective amount of a non-absorbed sodium-binding composition comprising a sodium-binding polymer, said polymer comprising at least one of polyvinylsulfonate polymer, polyvinylsulfamate polymer, polyvinylsulfamate/vinylsulfate copolymer, vinylphosphonate/acrylic acid copolymer,

polyvinylsulfate polymer, or crosslinked polyvinylsulfamate polymer, wherein said human subject is suffering from hypertension, chronic heart failure, end stage renal disease, liver cirrhosis, chronic renal insufficiency, fluid overload, or sodium overload.[1]

Independent claim 62 is directed to a method of removing sodium from a human subject comprising administering to a human subject in need thereof an effective amount of a non-absorbed sodium-binding composition comprising a sodium-binding polymer, said polymer comprising at least one of polyvinylsulfonate polymer, polyvinylsulfamate polymer, polyvinylsulfamate/vinylsulfate copolymer, vinylphosphonate/acrylic acid copolymer, polyvinylsulfate polymer, crosslinked polyvinylsulfamate polymer, or poly α-acrylic acid polymer, wherein said effective amount of sodium-binding composition administered is at least about 5 grams of polymer per day and said human subject is suffering from hypertension, chronic heart failure, end stage renal disease, liver cirrhosis, chronic renal insufficiency, fluid overload, or sodium overload.[2]

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Appellants appeal the rejection of claims 1, 13-15, 36-44, 49, and 60-76 under 35 U.S.C. § 112 as being nonenabled. Appellants further appeal the rejection of claims 1, 13-15, 36-44, 60 and 61 under 35 U.S.C. § 103(a) as being unpatentable over Martani (EP 039453) in view of Murugesan et al (US 5,846,990) and Notenbomer (EP 0 730 494).

VII. ARGUMENT

A. 35 U.S.C. § 112 Rejection

Claims 1, 13-15, 36-44, 49, and 60-76 satisfy the enablement requirement of 35 U.S.C. § 112, paragraph 1.

Claims 1 and 62

Reconsideration is respectfully requested of the rejection of claims 1, 13-15, 36-44, 49, and 60-76 as failing to satisfy the enablement requirement of 35 U.S.C. § 112, paragraph 1.

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[1] *See* specification at paragraph [0014] and original claim 16.
[2] *See* specification at original claims 1, 16, and 39 and paragraph [0019].

Independent claim 1 is summarized above. The Office states that while the specification is "enabling for counter ions of NH4, Ca, H, cross-linked co-polymers and homopolymers at 4 mmol/gm as measured in the feces of a human patient[s], [it] does not reasonably provide enablement for any of the polymers as now claimed at any level of Na-binding in the claimed syndromes."[3]

Applicants submit that the specification contains support sufficient to enable those skilled in the art to practice the inventions of claims 1, 13-15, 36-44, 49, and 60-76 without undue experimentation. The pharmaceutically active polymers of these claims are described in detail throughout the specification, particularly on pages 14-24, and methods of preparing these polymers are described, for example, on pages 24-25, and exemplified in Example 2 on pages 30-34. The specification also sets forth in detail the claimed methods of treatment on pages 25-27. All of these descriptions are written in clear and concise language using terms that are well-known to skilled persons.

Moreover, the specification describes on pages 6-14 and 25-27, that the polymers of the present claims remove sodium from the body by binding and removing the sodium from the gastrointestinal tract, that this sodium removal from the body affects the sodium concentration and water balance, and that the effect on sodium concentration and water balance has a beneficial effect for the claimed conditions. Although the Examiner states that the in vivo binding capacity of 4 mmol/g must be reinserted into claim 1, the requirement is repeatedly referred to as a preferred embodiment in paragraphs [0013] and [0016]. On pages 30 and 34-38, the specification details *in vitro* and *in vivo* tests to determine the activity of the pharmaceutical polymers. Further, the specification describes effective dosages and routes of administration on pages 27-30. These descriptions include the various modes by which the compounds can be administered to animals, the pharmaceutically acceptable forms in which they can be administered, and appropriate dosages for their administration. This information is sufficient to enable one skilled in the art to practice the inventions of the claims and accordingly, complies with the enablement requirement of 35 U.S.C. § 112.

A specification that contains a teaching of the manner and process of making and using the invention in terms that correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as an enabling disclosure unless there is

[3] See Office action dated November 25, 2009 at page 2.

reason to doubt the objective truth of the statements contained therein. As acknowledged in M.P.E.P. § 2164.04, the court in *In re Marzocchi* held that:

> "it is incumbent on the Patent Office whenever a rejection [for enablement] is made, to explain *why* it doubts the truth or accuracy of any statement in the supporting disclosure and to back up such assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement."[4]

In this case, the Examiner appears to be relying upon the breadth of the claims as a basis for doubting enablement. A rejection merely for breadth, however, is not appropriate, as explained in *In Re Borkowski*,[5] *In re Robins*,[6] and in *Marzocchi* itself. Here, except for asserting that a person of skill in the art cannot identify an effective amount, the Office has not provided cogent reasoning to doubt applicants' specification. Thus, the Office has not met its burden of showing a *prima facie* case of lack of enablement under 35 U.S.C. § 112.

Applicants are not required to provide chemical or biological data as long as a description of each claimed invention is provided in clear and concise terms sufficient to enable a skilled person to practice each invention. Additionally, experimental examples are not required to support the complete scope of the claim. As stated in *In re Goffe*,[7] an applicant should not be required to limit the claims to materials disclosed in the examples because "[t]o demand that the first to disclose shall limit his claims to what he has found will work or to materials which meet the guidelines specified for 'preferred' materials in a process such as the one herein involved would not serve the constitutional purpose of promoting progress in the useful arts."[8]

Furthermore, and in any event, the experimentation required to test for the effective amount of a cation exchange polymer for each condition is not undue because a person of ordinary skill would know how to test for this using the guidance provided in the specification and such testing would be routine. Thus, claims 1, 13-15, 36-44, 49, and 60-76 satisfy the enablement requirement of 35 U.S.C. § 112.

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[4] *In re Marzocchi*, 439 F.2d 220, 224, 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971).
[5] 422 F.2s 904, 164 U.S.P.Q. 642 (C.C.P.A. 1970).
[6] 429 F.2d 452, 166 U.S.P.Q. 552 (C.C.P.A. 1970).
[7] 542 F.2d 564, 567, 191 U.S.P.Q. 429, 431 (C.C.P.A. 1976).
[8] *See id.* at 431.

B. 35 U.S.C 103(a) Rejection

Reconsideration is requested of the rejection of claims 1, 13-15, 36-44, and 60-61 as unpatentable under 35 U.S.C. § 103(a) over EP 0349453 (Martani) in view of U.S. Patent No. 5,846,990 (Murugesan) and Notenbomer (EP 0730494). The Office asserts that Martani uses Eudragit polymers with added actives that would have removed sodium from a patient and that it would have been obvious that Martani discloses oral formulations but not the disease states. The disease states are said to be disclosed by Murugesan with associated drugs and polymers similar to Martani's polymers are said to be disclosed by Notenbomer, and supposedly the Notenbomer compositions are known to lower sodium levels.[9]

Applicants submit that the above rejection is in error for the following reasons.

As is well known, the determination of whether a claim is obvious within § 103(a), depends on at least four underlying factual issues set forth in *Graham v. John Deere Co. of Kansas City*[10]: (1) the scope and content of the prior art; (2) differences between the prior art and the claims at issue; (3) the level of ordinary skill in the pertinent art; and (4) evaluation of any relevant secondary considerations. In April 2007, the Supreme Court affirmed the *Graham* analysis as the framework for determining obviousness.[11]

In addressing the scope and content of the prior art, references are not pertinent to an obviousness inquiry if they are not from analogous art.[12] A reference is analogous art if: (1) the reference is from the same field of endeavor, regardless of the problem addressed, or (2) the reference is not within the inventor's field of endeavor, yet it is reasonably pertinent to the particular problem addressed by the inventor.

In *Clay*, the PTO asserted that the claimed invention and the Sydansk reference were analogous art because they were part of a common endeavor of "maximizing withdrawal of petroleum stored in petroleum reservoirs."[13] Sydansk taught the

> use of a gel in unconfined and irregular volumes within generally underground natural oil-bearing formation to channel flow in a desired direction; Clay teaches the introduction of gel to the confined dead volume of a man-made storage tank.[14]

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[9] See Office action dated November 25, 2009 at page 3.
[10] 383 U.S. 1, 17, 86 S.Ct. 684, 15 L.Ed.2d 545 (1966).
[11] *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1739 (2007).
[12] *In re Clay*, 23 U.S.P.Q.2d 1058, 1060 (Fed. Cir. 1992).
[13] *Id.*
[14] *Id.*

However, the Federal Circuit disagreed with the Office and held that Clay's field of endeavor was "*storage* of refined liquid hydrocarbons" and Sydansk's invention was directed to the "*extraction* of crude petroleum."

When a reference has the same purpose as the claimed invention, it relates to the same problem, and that fact supports use of that reference in an obviousness rejection; but when a reference has a purpose different from that to which the claimed invention is directed, one skilled in the foreign art might or might not have reason to modify for some alien purpose; but the artisan concerned with the inventor's problem would have no motivation to consider the reference at all, as a candidate for modification or otherwise.[15]

The purpose of the Martani patent is to develop compositions for the prolonged *release* of various cationic or anionic active ingredients. The cationic active ingredients are loaded on various anionic resins, particularly, polystyrene sulfonate resin and then the polystyrene sulfonate-active ingredient complex is coated with either an anionic (e.g., Eudragit® S) or preferably, a cationic (e.g., Eudragit® RL) polymer coating to delay the release of the active ingredient once administered. For anionic active ingredients, a cationic resin such as cholestyramine is used to complex the active ingredient and an anionic polymer coating (e.g., Eudragit® S) is used to coat the cholestyramine-active ingredient complex. Martani discloses acrylate/methacrylate copolymers (e.g., Eudragit), polystyrene sulfonate and poly(acrylic acid) (e.g., Carbomer) as cation exchange polymers. Martani would not have led a skilled person to contemplate binding sodium in the gastrointestinal tract since the problem the reference addressed was to prolong release of active agents in the gastrointestinal tract.

Further, even if the Martani compositions could have bound positive ions in the gastrointestinal tract, there are many differences between binding sodium and potassium even though they are similar target ions. These differences include variances in the relative and absolute amounts of sodium and potassium along the gastrointestinal tract; the amounts of sodium and potassium depending upon the condition suffered by the patient; and the selectivity of a cation exchange polymer for sodium and potassium ions.

The amount of sodium as compared to the amount of potassium available for binding will be different because the relative and absolute amounts of sodium and potassium in the gastrointestinal tract change depending on location (e.g., distance from the stomach).

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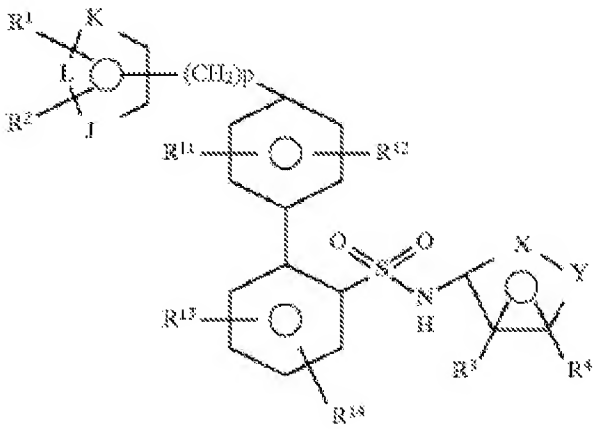
[15] *Id.*

Notenbomer recognizes this difference by relying on sodium being present in high amounts in comparison to the relatively low concentration of potassium (p. 3, lines 3-6). Also, Fordtran et al.,[16] studied the sodium and potassium concentrations in the upper GI after different meals, (see especially Figs 2, 4 and 10), found that at the end of the ileum, the sodium concentration is relatively high, whereas the potassium concentration is relatively low. However, at the end of the gastrointestinal tract, the contents have a relatively high potassium concentration and a relatively low sodium concentration.[17]

The reasoning that a skilled person would have been motivated to combine the Martani, Notenbomer, and Murugesan teachings to produce a method of removing sodium using the claimed polymers can be compared to that in *Clay*, where the PTO asserted that the claimed invention and the Sydansk reference were of a common endeavor because they were directed to "maximizing withdrawal of petroleum stored in petroleum reservoirs."[18] But in this case, the PTO articulates no reason why the Martani patent is analogous art to either the invention or Notenbomer or Murugesan. Applicants' endeavor is development of methods of removing sodium from the gastrointestinal tract to treat a range of conditions that are affected by high sodium levels.[19]

Murugesan discloses various small molecule sulfonamide compounds having the following formula:



[16] J.S. Fordtran et al. "Ionic Constituents and Osmolality of Gastric and Small-Intestinal Fluids after Eating," *Am. J. Digestive Dis.* **1966**, *11(7)*, 503.

[17] O. Wrong et al., "*In Vivo* Dialysis of Faeces as a Method of Stool Analysis," *Clin. Sci.* **1965**, *28*, 357-375. (see Figures 2 and 4).

[18] *Id.*

[19] *See* specification at paragraph [0013] and original claim 35.

These sulfonamides are described as endothelin antagonists useful to treat hypertension. While the Murugesan compounds are said to be useful to treat hypertension, a person of skill in the art would not have had a reason to combine the disclosure of Murugesan with Martani because the small molecules of the Murugesan sulfonamides are absorbed and act as endothelin antagonists. Such small molecule receptor antagonists' mechanism of action is to block the endothelin receptor sites to inhibit the effects of endothelin, an effective vasoconstrictor. In contrast, the sodium-binding polymers of the claimed invention are not absorbed from the gastrointestinal tract and they bind and remove sodium from the animal's system. One of ordinary skill would have had no more reason to combine Murugesan with Martani than to combine any other reference describing a compound useful for treating hypertension with Martani. Absent some reason to combine the disclosures of the cited references, no *prima facie* case of obviousness has been established.

Notenbomer generally discloses methods and particles for binding monovalent cations. The particles have a nucleus and a coating; the nucleus contains a cation exchange material and the coating comprises a membrane that is permeable for monovalent cations. This coating is disclosed as being more permeable for monovalent cations than for bi- or higher valent cations. Disclosed cation exchange polymers are polycarboxylates, polymaleinates, polyacrylates, polyacrylate-co-maleinates, polyphosphates, polysaccharides, cellulose, starch, pectins, alginate, and sulphonated polyvinylstyrenes. Exemplified cation exchange materials are polyphosphate and polystyrene sulfonate resins and exemplified coatings are cellulose acetate and polyethyleneimine. These particles can be used to treat hypertension. While the Office states that the reason the Martani, Murugesan and Notenbomer patents could be combined was to "provide acceptable application and improve the status of a patient in need thereof,"[20] this reason does not place Applicants' invention in the same field as the Martani or Murugesan patents nor does it address the problem disclosed in Applicants' specification or the still different problem discussed in the Notenbomer patent.

In arguendo, using Martani as the primary reference, the second step of the *Graham* analysis requires consideration of the differences between the prior art and the claims at issue. The Martani patent is described above and describes polymers used for prolonged release of active agents. Thus, the <u>difference</u> between the instant claims and Martani's prolonged release

[20] *See* Office action dated November 25, 2009 at page 4.

polymer particles is the specific polymers required by the claims (e.g., polyvinylsulfonate polymer, polyvinylsulfamate polymer, polyvinylsulfamate/vinylsulfate copolymer, vinylphosphonate/acrylic acid copolymer, polyvinylsulfate polymer, crosslinked polyvinylsulfamate polymer, or poly α-acrylic acid polymer) and the positive step of removing sodium from the gastrointestinal tract in a patient suffering from a particular condition.

Because the specific polymers were not disclosed in the Martani patent, the Examiner has recognized that the pending claims are not anticipated by the Martani patent. In formulating a rejection of the claims under § 103(a), the Examiner has found no art that relates to the problem to which the Martani patent relates, but instead has resorted to the Murugesan patent as disclosing the patient conditions, and forcibly combined the Murugesan patent with the Martani patent to support the assertion that pretty much any, but especially the claimed method of treatment by administering a sodium-binding polymer would have been obvious. Further, while the Office states that the specific polymers recited in instant claim 1 were disclosed in Notenbomer,[21] Notenbomer discloses polycarboxylates are useful, but claim 1 recites administration of poly-alpha-acrylic acid, which is much more specific and would not have been suggested by the disclosure of Notenbomer.

When the patent at issue claims a method of administering a chemical compound, the analysis of the *Graham f*actor i.e., the differences between the claimed invention and the prior art, can also turn on the structural similarities and differences between the compounds administered and the prior art compounds.[22] Obviousness based on structural similarity thus can be proved by identification of some motivation that would have led one of ordinary skill in the art to select and then modify a known compound (i.e. a lead compound) in a particular way to achieve the claimed compound.[23]

In *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.*,[24] the Federal Circuit addressed the obviousness issue for structurally similar chemical compounds. In *Takeda*, the claim at issue recited pioglitazone (5-{4-[2-(5-ethyl-2-pyridyl)ethoxy] benzyl}-2,4-thiazolidinedione.") having the following structure:

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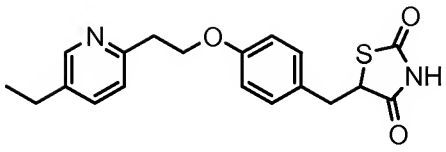
[21] See Office action dated November 25, 2009 at page 3.

[22] *See Eli Lilly & Co. v. Zenith Goldline Pharm., Inc.*, 471 F.3d 1369, 1377; 81 USPQ2d 1324 (Fed. Cir. 2006).

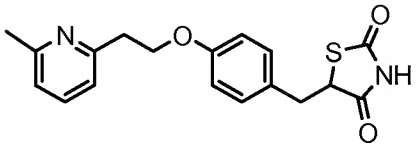
[23] *See Takeda Chem. Indus. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1356; 83 USPQ2d 1169 (Fed. Cir. 2007).

[24] 492 F.3d 1350 (Fed. Cir. 2007).



The ethyl substituent is attached to the 5-position on the pyridyl ring.

Alphapharm filed an ANDA to manufacture and sell a generic version of pioglitazone. According to Alphapharm, Takeda's claimed compound would have been obvious over the prior art compound TZD ("compound b": a pyridyl ring with a methyl (CH_3) group attached to the 6-position of the ring)[25], having the following structure:



Alphapharm argued that one of ordinary skill in the art would select compound b for antidiabetic research and then make "two obvious chemical changes: first, homologation, i.e., replacing the methyl group with an ethyl group, which would have resulted in a 6-ethyl compound; and second, 'ring-walking,' or moving the ethyl substituent to another position on the ring, the 5-position, thereby leading to the discovery of pioglitazone."[26]

The district court found, however, that one of ordinary skill in the art would not have selected compound b from the "hundreds of millions" of possible compounds. "[T]he prior art did not suggest to one of ordinary skill in the art that compound b would be the best candidate as the lead compound for antidiabetic research."[27] The Federal Circuit affirmed and held that there was no motivation to select a particular prior art compound (e.g., compound b) from the universe of prior art compounds and even if there was such a motivation, nothing in the prior art would have led a skilled person to modify compound b to arrive at the claimed compound. Thus, when determining the obviousness of new chemical compounds, there must be "some reason that would have led a chemist to modify a known compound in a particular manner to establish *prima facie* obviousness."[28]

Once a reason to modify a known compound is found, the skilled person must also have a reasonable expectation that such a modification will be successful or beneficial in some way. In

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[25] *Id.* at 1354.
[26] *Id.* at 1357.
[27] *Id.* at 1358.
[28] *Id.*

many chemical cases a "reasonable expectation of success" is not always found, as the Federal Circuit stated in *Eisai Co. v. Dr. Reddy's Laboratories, Inc.*[29] :

> First, KSR assumes a starting reference point or points in the art, prior to the time of invention, from which a skilled artisan might identify a problem and pursue potential solutions. Second, KSR presupposes that the record up to the time of invention would give some reasons, available within the knowledge of one of skill in the art, to make particular modifications to achieve the claimed compound. See Takeda Chem. Indus. v. Alphapharm Pty., Ltd., 492 F.3d 1350, 1356 (Fed. Cir. 2007). ("Thus, in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound."). Third, the Supreme Court's analysis in KSR presumes that the record before the time of invention would supply some reasons for narrowing the prior art universe to a "finite number of identified, predictable solutions," 127 S. Ct. at 1742. In Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories, Inc., 520 F.3d 1358, 1364 (Fed. Cir. 2008), this court further explained that this "easily traversed, small and finite number of alternatives . . . might support an inference of obviousness." To the extent an art is unpredictable, as the chemical arts often are, KSR's focus on these "identified, predictable solutions" may present a difficult hurdle because potential solutions are less likely to be genuinely predictable. (Emphasis added)

As *KSR v. Teleflex* and *Takeda v. Alphapharm* emphasize, it is important to "identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does."[30] There is no reason for the forced combination.

As another instructive example, consider *Procter & Gamble Co. v. Teva Pharmaceuticals*,[31] where risedronate, a bisphosphonate which is a bone resorption inhibitor, was the subject of the challenged claims. Risedronate and its closest prior art compound, 2-pyrEHDP are shown below. Risedronate and 2-pyrEHDP are positional isomers.

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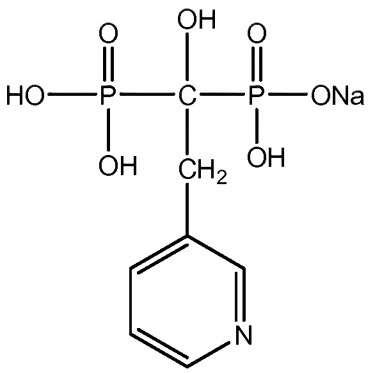
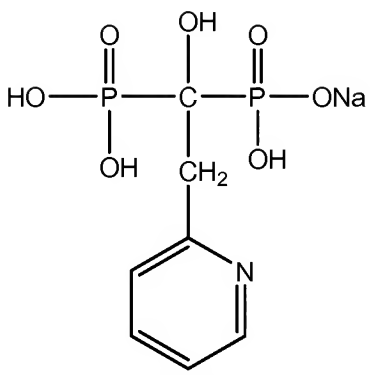
[29] *Eisai Co. v. Dr. Reddy's Laboratories, Inc.*, 87 U.S.P.Q.2d 1452 (Fed. Cir. 2008).

[30] *KSR v. Teleflex, Inc.*, 82 U.S.P.Q.2d 1385, 1396.

[31] 566 F.3d 989, 90 U.S.P.Q.2d 1947 (Fed. Cir. 2009).



risedronate



2-pyrEHDP

Although Teva argued that a chemist would have conceived of the positional isomers, the court held that due to the positional change of the nitrogen atom, the isomers differ in three dimensional shape, charge distribution, and hydrogen bonding properties and hence are not obvious over each other. Further, there was evidence that the bisphosphonate art was unpredictable, so there was no reasonable expectation that a modification would have been successful.

Just like Alphapharm in *Takeda*, the PTO is arguing that it would have been obvious to one of ordinary skill in the art to choose the specific sodium-binding polymers disclosed in Notenbomer from the millions of possible available cation exchange polymers in the prior art because they can bind sodium. As *KSR v. Teleflex* and *Takeda v. Alphapharm* emphasize, it is important to "identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does."[32] Although the Office states that the references would have been combined to "provide acceptable application and improve the status of a patient in need thereof,"[33] similar to *Ex parte Meagher*, such a general statement for the reason for combining the references does not address the specific claim elements, e.g., why one would select the Murugesan or Notenbomer patents from the multitude of references describing either hypertension treatment or cation exchange polymers useful to bind sodium.[34] The question is not whether there is a reason to make an improvement.

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[32] *KSR v. Teleflex, Inc.*, 82 U.S.P.Q.2d 1385, 1396.

[33] Office action dated November 25, 2009 at page 4.

[34] *Ex parte Meagher*, Appeal no. 2008-3613; Application No. 10/380,898 decided September 22, 2008 at page 15 (describing that combining references for the purpose of "obtaining a conversion coating having good corrosion resistance and good top coat adhesion properties-which are likely goals of virtually every conversion coating composition-do not provide the ordinary coating formulations chemist with a reason to systematically vary" the prior art compositions to arrive at the claimed composition.).

That is essentially always the case. The question is whether there is a reason to make a particular modification, and if so, whether there is any expectation of an improvement.

The Office has not provided a reason for the modification of the particular sodium-binding polymers with enough particularity to establish a *prima facie* case of obviousness. Further, there is no reason provided in the cited art or reliance on knowledge in the art that would have led a skilled person to select the cation exchange polymers from Martani, the condition of hypertension from Murugesan, and the ability of the polymers to bind sodium from Notenbomer to arrive at the methods for removing sodium required by claim 1 and 62.

Applicants submit that the PTO is engaging in the exact hindsight bias that the Court has repeatedly urged must be avoided. The PTO has not provided a reason why a skilled person would choose the teachings from the cited references to arrive at the claimed methods. Hence, the only way that the PTO could arrive at this conclusion is based on the teachings of the instant application while disregarding what the art would have actually led a skilled person to do.

The PTO has failed to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed invention does. There is simply no reason that a skilled person would have combined the Martani, Murugesan, and Notenbomer patents to arrive at the claimed invention.

Finally, the office asserts that there are "no unobvious and/or unexpected results obtained" because the prior art discloses use of cation exchange polymers.[35] However, as detailed above, the Office has failed to establish a *prima facie* case of obviousness because it has provided no reason why a skilled person would have combined the cited references to arrive at the claimed methods. Since no *prima facie* case of obviousness has been established, applicant need not show unexpected results. Thus, claims 1, 13-15, 36-44, and 60-61 are patentable over EP 0349453 (Martani) in view of U.S. Patent No. 5,846,990 (Murugesan) and EP 0730494 (Notenbomer) under 35 U.S.C. § 103(a).

In sum, claims 13-15, 36-44, and 60-61 depend directly or indirectly from claim 1 and are patentable over the cited references under 35 U.S.C. § 103(a) for at least the same reasons as claim 1.

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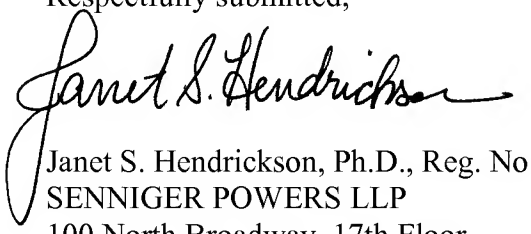
[35] Office action dated November 25, 2009 at page 4.

VIII. CONCLUSION

For the reasons stated above, Appellants respectfully request that the Office's 35 U.S.C. § 112 rejection of claims 1, 13-15, 36-44, and 60-76 and 35 U.S.C. § 103(a) obviousness rejection of claims 1, 13-15, 36-44, and 60-61 be reversed.

The Commissioner is hereby authorized to charge any additional fees which may be required to Deposit Account No. 19-1345.

Respectfully submitted,



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IX. CLAIMS APPENDIX

1. A method of removing sodium from a human subject comprising administering to a human subject in need thereof an effective amount of a non-absorbed sodium-binding composition comprising a sodium-binding polymer, said polymer comprising at least one of polyvinylsulfonate polymer, polyvinylsulfamate polymer, polyvinylsulfamate/vinylsulfate copolymer, vinylphosphonate/acrylic acid copolymer, polyvinylsulfate polymer, or crosslinked polyvinylsulfamate polymer, wherein said human subject is suffering from hypertension, chronic heart failure, end stage renal disease, liver cirrhosis, chronic renal insufficiency, fluid overload, or sodium overload.

2. (Canceled)

3. The method of claim 1 wherein said sodium-binding composition exhibits decreased permeability to sodium bound in a lower gastrointestinal tract relative to a permeability exhibited by the sodium-binding composition to said bound sodium in an upper gastrointestinal tract.

4. (Canceled)

5. The method of claim 1 wherein said sodium-binding composition swells in an isotonic fluid environment.

6. The method of claim 1 wherein said sodium binding by said sodium-binding composition is dependent on a pH of an environment surrounding said polymeric composition.

7. The method of claim 3 wherein said sodium binding by said sodium-binding composition is dependent on a concentration of bile acids and/or fatty acids in an environment surrounding said polymeric composition.

8. The method of claim 3 wherein said sodium binding by said sodium-binding composition is dependent on an activity of enteric enzymes in an environment surrounding said polymeric composition.

9. The method of claim 1 wherein said sodium-binding composition comprises sulfonate or phosphonic polymers.

10. The method of claim 1 wherein said sodium-binding composition does not release Cl^- or OH^-.

11. The method of claim 1 wherein said sodium-binding composition does not release K^+.

12. (Canceled)

13. The method of claim 1 wherein said sodium-binding polymer comprises repeat units charged with H^+ or NH_4^+ ions.

14. The method of claim 1 wherein said effective amount of sodium-binding composition administered is from about 0.5 grams per day to about 25 grams per day.

15. The method of claim 1 wherein the effective amount of said sodium-binding composition removes about 50 mmol of sodium per day.

Claims 16 - 35. (Canceled)

36. The method of claim 1 wherein extra cellular water is removed from said human subject.

37. The method of claim 1 wherein a beneficial effect is observed on fluid management, blood pressure control, and/or interdialytic weight gain.

38. The method of claim 1 wherein said human subject is suffering from a disease characterized by a presence of abnormal quantities of sodium and/or water in the body of said human subject.

39. The method of claim 1 wherein said human subject is resistant to diuretic treatment.

40. The method of claim 1 wherein sodium is removed from the human subject over an extended period of time.

41. The method of claim 1 wherein treatment of said human subject reduces the incidence of edema after a cardiac event.

42. The method of claim 1 wherein said human subject is suffering from volume/salt sensitive diastolic heart failure.

43. The method of claim 1 wherein said composition is co-administered with a diuretic, an ACE inhibitor, an α- blocker, a β- blocker, an angiotensin II receptor blocker, or a combination thereof.

44. The method of claim 1 wherein said composition is co-administered with a laxative.

45. The method of claim 1 wherein said sodium-binding polymer has an *in vitro* sodium binding capacity of equal to or more than 6 mmol per gram of polymer at a pH of about 7.5.

46. The method of claim 49 wherein the *in vivo* sodium binding capacity is 5 mmol or more per gram of said polymer.

47. The method of claim 49 wherein the *in vivo* sodium binding capacity is 6 mmol or more per gram of said polymer.

48. The method of claim 49 wherein the *in vivo* sodium binding capacity is 8 mmol or more per gram of said polymer.

49. The method of claim 1 wherein the *in vivo* sodium binding capacity is 4 mmol or more per gram of polymer and is calculated by measuring the amount of sodium in the feces after administration of the sodium-binding polymer to a human patient.

50. (Canceled)

51. The method of claim 1 wherein said sodium binding polymer comprises a crosslinked polymer.

Claims 52 - 59. (Canceled)

60. The method of claim 1 wherein said human subject is suffering from end stage renal disease.

61. The method of claim 1 wherein said human subject is suffering from chronic heart failure.

62. A method of removing sodium from a human subject comprising administering to a human subject in need thereof an effective amount of a non-absorbed sodium-binding composition comprising a sodium-binding polymer, said polymer comprising at least one of polyvinylsulfonate polymer, polyvinylsulfamate polymer, polyvinylsulfamate/vinylsulfate copolymer, vinylphosphonate/acrylic acid copolymer, polyvinylsulfate polymer, crosslinked polyvinylsulfamate polymer, or poly α-acrylic acid polymer,

wherein said effective amount of sodium-binding composition administered is at least about 5 grams of polymer per day and said human subject is suffering from hypertension, chronic heart failure, end stage renal disease, liver cirrhosis, chronic renal insufficiency, fluid overload, or sodium overload.

63. The method of claim 62 wherein said sodium-binding composition comprises sulfonate or phosphonic polymers.

64. The method of claim 62 wherein extracellular water is removed from said human subject.

65. The method of claim 62 wherein a beneficial effect is observed on fluid management, blood pressure control, and/or interdialytic weight gain.

66. The method of claim 62 wherein said human subject is suffering from a disease characterized by a presence of abnormal quantities of sodium and/or water in the body of said human subject.

67. The method of claim 62 wherein said human subject is resistant to diuretic treatment.

68. The method of claim 62 wherein sodium is removed from the human subject over an extended period of time.

69. The method of claim 62 wherein treatment of said human subject reduces the incidence of edema after a cardiac event.

70. The method of claim 62 wherein said human subject is suffering from volume/salt sensitive diastolic heart failure.

71. The method of claim 62 wherein said composition is co-administered with a diuretic, an ACE inhibitor, an α- blocker, a β- blocker, an angiotensin II receptor blocker, or a combination thereof.

72. The method of claim 62 wherein the *in vivo* sodium binding capacity is 4 mmol or more per gram of polymer and is calculated by measuring the amount of sodium in the feces after administration of the sodium-binding polymer to a human patient.

73. The method of claim 62 wherein said polymer comprises at least one of polyvinylsulfonate polymer, polyvinylsulfamate polymer, polyvinylsulfamate/vinylsulfate copolymer, vinylphosphonate/acrylic acid copolymer, polyvinylsulfate polymer, or crosslinked polyvinylsulfamate polymer.

74. The method of claim 62 wherein said sodium binding polymer comprises a crosslinked polymer.

75. The method of claim 62 wherein said human subject is suffering from end stage renal disease.

76. The method of claim 62 wherein said human subject is suffering from chronic heart failure.

X. EVIDENCE APPENDIX

None.

XI. RELATED PROCEEDINGS APPENDIX

None.